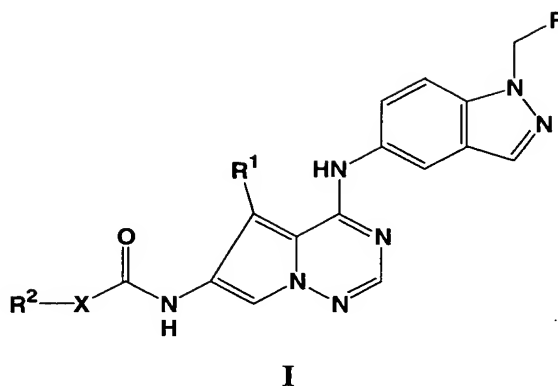


What is Claimed is:

1. A compound of formula I



wherein

R is selected from the group consisting of aryl, substituted aryl, heterocyclo, and substituted heterocyclo;

R¹ is selected from the group consisting of alkyl and substituted alkyl;

R² is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, aralkyl, heterocyclo, and substituted heterocyclo; or, R² may be absent;

X is selected from the group consisting of a bond, O, S, C(R³)₂, C(R³)₃, NR³; and N(R³)₂;

R³ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, heterocyclo, and substituted heterocyclo, and pharmaceutically acceptable salts, prodrugs, enantiomers, diastereomers, and solvates thereof.

2. The compound according to claim 1 wherein R is aryl or substituted aryl and R¹ is a lower alkyl group.

3. The compound according to claim 2 wherein X is -O- and R² is cycloalkyl, substituted cycloalkyl, heterocyclo or substituted heterocyclo.

4. The compound according to claim 3 wherein R is phenyl or substituted phenyl and R¹ is methyl or ethyl.

5. A compound selected from the group consisting of
- 5 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2R)-2-pyrrolidinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2S)-2-pyrrolidinylmethyl ester,
- 10 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3R)-3-morpholinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, 3-[(3S)-3-hydroxy-1-pyrrolidinyl] propyl ester,
- 15 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, 3-[(3S)-3-hydroxy-1-piperidinyl] propyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3R)-3-pyrrolidinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, 3-[(3R)-3-hydroxy-1-pyrrolidinyl] propyl ester,
- 20 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, [(2S)-1-methyl-2-pyrrolidinyl] methyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2S)-2-morpholinylmethyl ester,
- 25 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-pyrrolidinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2R)-2-morpholinylmethyl ester,
- [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, [(3R)-1-methyl-3-pyrrolidinyl] methyl ester,
- 30 [5-ethyl-4-[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, trans-4-aminocyclohexyl ester,

- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3R)-3-piperidinyl ester,
- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-piperidinyl ester,
- 5 [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, cis-4-aminocyclohexyl ,
- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2R,4R)-2 -(hydroxymethyl)-4-piperidinyl ester,
- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2S)-2 -(hydroxymethyl)-4-piperidinyl ester,
- 10 [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, cis-4-(aminomethyl)cyclohexyl ester,
- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, cis-4-amino-4-methylcyclohexyl ester,
- 15 [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, [(2R,4R)-4 -(hydroxy-2-piperidinyl)methylester,
- [5-ethyl-4-[[[(1-phenylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, trans-4-(aminomethyl)cyclohexyl ester,
- [5-ethyl-4-[[1-(2-oxazolylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- 20 [5-ethyl-4-[[1-(2-thienylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- [5-ethyl-4-[[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- 25 [5-ethyl-4-[[1-(4-thiazolylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- [5-ethyl-4-[[1-(3-thienylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- [5-ethyl-4-[[1-(2-pyridinylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- 30 [5-ethyl-4-[[1-(2-thiazolylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,

- [5-ethyl-4-[[1-(3-pyridinylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- [5-ethyl-4-[[1-(pyrazinylmethyl)-1H-indazol-5-yl]amino]pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- 5 [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, trans-4-aminocyclohexyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2R,4R)-2-(hydroxymethyl)-4-piperidinyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2S,4S)-2-(hydroxymethyl)-4-piperidinyl ester,
- 10 [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, cis-4-aminocyclohexyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, cis-4-amino-4-methyl-cyclohexyl ester,
- 15 [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2R)-2-aminopropyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (2S)-2-aminopropyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-morpholinylmethyl ester,
- 20 [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3R)-3-piperidinyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3S)-3-piperidinyl ester,
- 25 3-[[[[[4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-yl]amino]-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yl]amino]carbonyl]oxy]methyl]-4-morpholinecarboxylic acid, (3S)-1,1-dimethylethyl ester,
- [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, 3-morpholinylmethyl ester, and
- 30 [4-[[1-(3-fluorophenyl)methyl]-1H-indazol-5-ylamino]-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yl]-carbamic acid, (3R)-3-morpholinylmethyl ester.

6. A compound of claim 1 having an IC_{50} value of less than 5 μM for HER kinase assay selected from the group consisting of HER1, HER2 and HER4.
7. A compound of claim 1 having an IC_{50} value of less than 1 μM for
5 HER kinase assay selected from the group consisting of HER1, HER2 and HER4.
8. A compound of claim 1 having an IC_{50} value of less than 0.1 μM for HER kinase assay selected from the group consisting of HER1, HER2 and HER4.
- 10 9. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
10. A pharmaceutical composition comprising a compound of claim 1 in combination with a pharmaceutically acceptable carrier and at least one other anti-
15 cancer or cytotoxic agent formulated as a fixed dose.
11. The pharmaceutical composition of Claim 10 wherein said anti-cancer or cytotoxic agent is selected from the group consisting of tamoxifen, toremifene, raloxifene, droloxifene, idoxifene, megestrol acetate, anastrozole, letrozole, borazole,
20 exemestane, flutamide, nilutamide, bicalutamide, cyproterone acetate, gosereline acetate, leuprolide, finasteride, metalloproteinase inhibitors, inhibitors of urokinase plasminogen activator receptor function, inhibitors of insulin growth receptor, growth factor antibodies, growth factor receptor antibodies, bevacizumab, cetuximab, tyrosine kinase inhibitors, serine/threonine kinase inhibitors, methotrexate, 5-fluorouracil,
25 purine and adenosine analogues, cytosine arabinoside, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin, mithramycin, cisplatin, carboplatin, nitrogen mustard, melphalan, chlorambucil, busulphan, cyclophosphamide, ifosfamide, nitrosoureas, thiotepa, vincristine, vinorelbine, vinblastine, vinflunine paclitaxel, docetaxel, epothilone analogs, discodermolide
30 analogs, eleutherobin analogs, etoposide, teniposide, amsacrine, topotecan, irinotecan, flavopyridols, proteasome inhibitors including bortezomib and biological response modifiers.

12. A method for treating a proliferative disease, comprising administering to a warm-blooded species in need thereof, a therapeutically effective amount of a compound of claim 1.

5 13. The method of claim 12 wherein the proliferative disease is selected from the group consisting of cancer, psoriasis and rheumatoid arthritis.

14. The method of claim 13 wherein the proliferative disease is cancer.

10 15. The method of claim 14 further comprising administering to a warm-blooded species in need thereof, a therapeutically effective amount of at least one other anti-cancer or cytotoxic agent in combination with a compound of claim 1.

15 16. The method of claim 15 wherein said anti-cancer or cytotoxic agent is selected from the group consisting of tamoxifen, toremifene, raloxifene, droloxifene, iodoxifene, megestrol acetate, anastrozole, letrozole, borazole, exemestane, flutamide, nilutamide, bicalutamide, cyproterone acetate, gosereline acetate, leuprolide, finasteride, metalloproteinase inhibitors, inhibitors of urokinase plasminogen activator receptor function, inhibitors of insulin growth receptor, growth factor antibodies, growth factor receptor antibodies, bevacizumab, cetuximab, tyrosine kinase inhibitors, serine/threonine kinase inhibitors, methotrexate, 5-fluorouracil, purine and adenosine analogues, cytosine arabinoside, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin, mithramycin, cisplatin, carboplatin, nitrogen mustard, melphalan, chlorambucil, busulphan, cyclophosphamide, ifosfamide, nitrosoureas, 20 thiotepa, vincristine, vinorelbine, vinblastine, vinflunine paclitaxel, docetaxel, epothilone analogs, discodermolide analogs, eleutherobin analogs, etoposide, teniposide, amsacrine, topotecan, irinotecan, flavopyridols, proteasome inhibitors including bortezomib and biological response modifiers.

30 17. A method of modulating receptor tyrosine kinase activity which comprises administering to a warm blooded species in need thereof, an effective amount of a compound of claim 1.

18. The method of claim 17 wherein said receptor tyrosine kinase is selected from the group consisting of HER1, HER2 and HER4.

5 19. A method for treating diseases associated with signal transduction pathways operating through growth factor receptors, which comprises administering to a warm-blooded species in need thereof a therapeutically effective amount of a compound of claim 1.